

# The quandary of Creutzfeldt–Jakob disease

Bryce Larke, MD, CM, DCISc

Why is there such controversy and uncertainty over whether to notify recipients of blood products that may have been contaminated with the infectious agent associated with Creutzfeldt–Jakob disease (CJD)?<sup>1</sup> Notification programs for recipients of blood contaminated with hepatitis C virus or HIV are widely acknowledged, by both health care professionals and the public, as beneficial. These programs, called “look-backs,” allow individual recipients and their sexual or other close contacts, who might otherwise remain unaware of their possible infection, the opportunity to access counselling, therapeutic interventions, and additional medical and social support services.

What is so different about CJD, an often misspelled clinical entity that many physicians might only vaguely recall from their student lectures on neuropathology?

First, CJD is rare. The incidence of CJD in Canada and other developed countries has been stable at about one per million population annually over a long period, even after the widespread introduction of blood transfusion and use of albumin.<sup>2–4</sup> Most medical practitioners will never see a patient with CJD in their lifetime.

Second, there is no direct evidence of CJD transmission through blood transfusion. Readers of *CMAJ* have been well-served by several excellent articles on the transmissible spongiform encephalopathies, which include CJD, “mad cow disease” in Europe and its recently recognized human counterpart, new variant CJD (nvCJD).<sup>2,5–7</sup> There is conclusive evidence that many infectious agents — bacteria, protozoa and viruses — can be transmitted from human to human through transfusion of cellular blood components, plasma and fractionated blood products.<sup>8</sup> However, reviews of the world’s scientific literature have provided no direct evidence that CJD or nvCJD, caused by prions, has been transmitted through the blood supply. The risk, at present, is appropriately regarded as theoretical, although debate continues.<sup>1,7,9–14</sup> There is no question that the emergence of nvCJD in the United Kingdom, first reported in 1996, has turned up the heat on this debate. The infectious agent associated with nvCJD has crossed species barriers, has been recovered from human tonsillar tissue and has tropism for B lymphocytes. But nvCJD has not been detected in Canada or the United States, and the prion associated with CJD does not have the more ominous biological characteristics of nvCJD.

If the risk of CJD being transmitted through blood is only theoretical, why are clinicians, bioethicists, lawyers and government regulatory authorities actively engaged in debate focusing on CJD and the blood system? The Krever inquiry is having a continuing impact not only on the Canadian blood system but also on many other aspects of clinical practice.<sup>15,16</sup> Perhaps most problematic is the question of whether to notify individual recipients of blood products fractionated from plasma pools involving a donor later diagnosed with CJD. If recipients are to be notified, how is the notification best carried out and by whom? Can harm result from notification? In considering these questions it should be kept in mind that decisions about many of the issues discussed in this editorial were first made shortly after a massive withdrawal of blood products in Canada in the summer of 1995, *before* the recognition of nvCJD in the United Kingdom added further uncertainty.<sup>2,5,6</sup>

In Canada regulatory measures regarding CJD are in place to protect recipi-



## Editorial

## Éditorial

**Dr. Larke is a Professor in the Department of Pediatrics, University of Alberta, Edmonton, Alta. He is on secondment to Alberta Health and the Canadian Blood Services, Edmonton, Alta.**

*The views expressed here are those of the author and not the University of Alberta, Alberta Health or the Canadian Blood Services.*

*CMAJ* 1998;159:789–92

‡ See related articles pages 771 and 829



ents of blood and blood products. If a person with CJD or at risk for CJD is found to have donated blood, consignees (hospitals and public health clinics) of the blood products involved are alerted to withdraw and quarantine any remaining stored product.<sup>10</sup>

It is interesting to note that the US recently revised its policy on the withdrawal of plasma derivatives associated with CJD. The Surgeon General announced in August 1998 that the US will *discontinue* withdrawals in situations where a donor has been diagnosed with, or has risk factors for, classical CJD. Withdrawals will be required only if a donor is diagnosed with nvCJD.<sup>17</sup>

Why are we bothering with notification? In addition to the lack of direct evidence that CJD can be transmitted through blood, there are no laboratory tests to determine if a recalled blood product is actually contaminated with the CJD agent or if the recipient has acquired the infection.<sup>7,10</sup> Furthermore, there are no prophylactic interventions or treatments of benefit to the recipient and no precautions or lifestyle changes that could be recommended to avoid possible spread to sexual contacts or to future offspring.<sup>1</sup> Since there are few, if any, tangible benefits for the recipient in a CJD look-back program, many people might prefer not to be burdened with this knowledge. Perhaps health care professionals have overreacted in an attempt to avoid being paternalistic and making decisions about what patients should or should not be told.

A consensus conference held in Toronto in June 1996, appropriately entitled "Decision-making in times of uncertainty," sought to resolve some of the difficult issues related to CJD.<sup>18</sup> A second conference, subtitled "Recall, withdrawal, notification and recipient notification," took place in Ottawa on June 1 and 2 of this year.<sup>19</sup> The following questions were among those raised at the 1998 conference: Do patients want to be notified of possible exposure to CJD? Is there a duty to notify? What is the responsibility of the patient's personal physician in this dilemma? Among those offering some answers to these questions was Dr. Susan King. In this issue (page 771) King and her colleagues relate their experience with notifying pediatric patients (or their parents) who had received blood products that were subsequently recalled (between July 1995 and February 1996) because of possible contamination with the CJD agent. Playing an important role in their decision to notify individual recipients was a group of parents of the children involved. Investigators at the Hospital for Sick Children in Toronto administered a questionnaire to the families of the patients several weeks after they received letters of notification from the hospital. Eighty-one percent of the respondents said they wanted to be notified of the possible risk of CJD, despite initial reactions of anxiety, fear and anger. Over 50 percent of respondents indicated that their current physician

should be the one to give them the information or should be involved with the notification process.

A similar experience with another CJD notification program was presented at the Ottawa conference by Dr. John Freedman.<sup>20</sup> Following an extensive decision-making process at St. Michael's Hospital in Toronto, letters were sent to the hospital's attending "physician of record" for each patient who had received the implicated blood products, strongly recommending that he or she inform the recipient of the possible risk of exposure to CJD. When followed up the next year, about 80% of the patients who had been contacted were grateful for the notification; a number of them volunteered that they would have preferred that the letter or other information come from their family doctor.

The experience of these 2 Toronto hospitals, as well as other presentations at the conference, left those in attendance with the impression that most patients favoured being notified about possible exposure to CJD. But what about the other recipients, approximately 20% of those questioned? Among patients or their parents who have been included in CJD look-back programs, opinion is sharply divided on the merits of being notified, as Barbara Sibbald describes on page 829 of this issue. For some, it has been a very negative experience and, in the absence of evidence of transmission of CJD through blood, is seen as an injustice. However, even for the recipients who are most insistent on and supportive of patient notification, there may be a harmful outcome. Sibbald relates the consternation of one Calgary physician, who was invited to a meeting of the Canadian CJD Society, a local support group that includes a number of recipients identified in the 1995 recall of blood products. According to her article, some members of the society seriously believe that several of the recipients are already showing preliminary clinical manifestations of CJD. These people almost certainly do not have early CJD but rather the problems of waning intellectual, visual and locomotor capacity that often accompany the natural aging process. If this sad tale is correct, other physicians will likely come to share the concerns of the Calgary practitioner and to question the wisdom of notifying individual recipients.

Physicians may be divided on the notification issue, but do they have a *duty* to inform their patients about possible exposure to CJD? A follow-up study a year after St. Michael's Hospital launched its look-back program revealed that nearly 29% of the attending physicians had not notified their patients.<sup>20</sup> Have these practitioners been placed in an ethical and legal dilemma because they neglected or deliberately chose not to notify their patients, despite strong recommendations from the hospital to do so? Although Freedman did not present an analysis of the reasons why the physicians acted as they did, it seems rea-



sonable to assume that some may not have shared the viewpoint, tinged perhaps by legal concerns, of the St. Michael's Hospital authorities who had ruled in favour of individual recipient notification. Physicians who make a conscientious decision not to inform their patients of the theoretical risks of exposure to CJD through blood products have some respectable support for their stance. In a scholarly article by clinicians, bioethicists and legal experts,<sup>1</sup> it was argued that individual notification is currently not justified.

If patients who have possibly been exposed to CJD through blood products, as well as health care professionals, ethicists and lawyers, remain uncertain about the topics discussed at the June 1998 CJD conference, how does industry view the debate? Apart from the major economic impact of recalling millions of dollars' worth of fractionated blood products, a sizeable portion of the recent global shortage of these vital therapeutic agents can be attributed to the destruction of various plasma pools or recall of finished products by the fractionation industry after it learned that a donor had been diagnosed with CJD or was at risk for CJD.<sup>3</sup> To assist in dealing with the complex challenges faced by the industry, Canada's largest supplier of fractionated blood products, Bayer Inc., has established a scientific and ethical advisory council of highly qualified individuals, headed by Dr. Burleigh Trevor-Deutsch, a lawyer and ethicist at the University of Ottawa. Among the first items on its agenda, the advisory council is wrestling with concerns about notification of recipients of blood products that may have been contaminated with the CJD agent. Their recommendations on this thorny issue are expected this fall and will apparently be open to public scrutiny.<sup>21</sup>

Whether or not the scientific and ethical advisory council favours individual recipient notification, much of the future burden of informing patients about the potential risks of exposure to CJD through blood products will likely fall upon general practitioners. In both of the Toronto hospital look-back studies mentioned above, recipients expressed a preference for involving their own doctor in the notification process. Although the 2 recipients interviewed by Sibbald had opposing viewpoints on most aspects of the notification issue, they did agree that general practitioners should be better informed about the disease. Most physicians probably consider themselves inadequately prepared to deal with the complexities presented by CJD. There is a large task ahead to better educate health care professionals as well as the general public, not only about CJD and the pros and cons of various notification strategies, but also about the balance between the benefits and other hazards of blood transfusion.<sup>8</sup> Trevor-Deutsch was challenged at the June 1998 conference to include, in the recommendations of the advisory council, some provision for adequate financial and human

resources to enable medical practitioners to fulfil whatever future role they may be called upon or choose to play as the CJD saga unfolds.

In a publication dealing with various concerns related to the safety of the blood supply, AuBuchon and colleagues<sup>22</sup> stated, "Although physicians must continue to advocate the most effective care available for patients, they must also keep decision makers abreast of the effects of societal decisions that may have been made more on the basis of fear and emotion than logically defined benefits." Canadian medical practitioners are already seeing the effects of CJD look-back programs. Physicians can have a major impact on public opinion and the shaping of rational policies regarding CJD issues, but they must be included early in the decision-making process and given adequate resources and appropriate incentives to meet this challenge. More specifically, physicians must be given opportunities to attend continuing medical education courses that deal with CJD and other blood safety concerns. And they must be paid for the time they spend counselling anxious patients and their families whose lives may have been thrown into sudden turmoil through a decision, wise or unwise, to alert them to the potential risks of exposure to CJD through blood products. Only through these measures can physicians fulfil their integral role as both patient advocates and barometers of public opinion.

Disclosure: Dr. Larke is employed on a contractual basis with both Canadian Blood Services and Alberta Health.

## References

1. Caulfield T, Dossetor J, Boshkov L, Hannon J, Sawyer D, Robertson G. Notifying patients exposed to blood products associated with Creutzfeldt-Jakob disease: integrating science, legal duties and ethical mandates. *CMAJ* 1997; 157(10):1389-92.
2. MacKnight C, Rockwood K. Bovine spongiform encephalopathy and Creutzfeldt-Jakob disease: implications for physicians. *CMAJ* 1996;155(5): 529-36.
3. Dodd RY, Sullivan MT. Creutzfeldt-Jakob disease and transfusion safety: tilting at icebergs? [editorial]. *Transfusion* 1998;38:221-3.
4. Ricketts MN, Cashman NR, Stratton EE, ElSaadany S. Is Creutzfeldt-Jakob disease transmitted in blood? *Emerg Infect Dis* 1997;3(2):155-63.
5. Dodelet V, Ricketts M, Cashman NR. Emerging problems in prion disease [editorial]. *CMAJ* 1996;155(5):549-51.
6. Vaughan P. Creutzfeldt-Jakob disease latest unknown in struggle to restore faith in blood supply. *CMAJ* 1996;155(5):565-8.
7. Cashman NR. A prion primer. *CMAJ* 1997;157(10):1381-5.
8. Guidelines for red blood cell and plasma transfusion for adults and children. Report of the Expert Working Group. *CMAJ* 1997;156(11):S1-S24 [supplement].
9. van Duijn CM, Delasnerie-Laupretre N, Masullo C, Zerr I, de Silva R, Wientjens DPWM, et al. Case-control study of risk factors of Creutzfeldt-Jakob disease in Europe during 1993-95. *Lancet* 1998;351:1081-5.



10. Ricketts MN. Is Creutzfeldt-Jakob disease transmitted in blood? Is the absence of evidence of risk evidence of the absence of risk? [editorial]. *CMAJ* 1997;157(10):1367-70.
11. Giulivi A. Can CJD be transmitted through the blood supply? [letter]. *CMAJ* 1998;158(6):714.
12. Larke B. Can CJD be transmitted through the blood supply? [letter]. *CMAJ* 1998;158(6):714-5.
13. Hoey J. Can CJD be transmitted through the blood supply? [letter]. *CMAJ* 1998;158(6):715-6.
14. Rohwer RG. Can CJD be transmitted through the blood supply? [letter]. *CMAJ* 1998;158(6):716-7.
15. Hoey J. The sensibility of safety: reflections on the Krever inquiry's final report [editorial]. *CMAJ* 1998;158(1):59-60.
16. Capen K. There's more to Krever's report than the blood issue — much more. *CMAJ* 1998;158(1):92-4.
17. American Association of Blood Banks. Surgeon General announces revised CJD withdrawal guidelines. AABB Faxnet no 378, 1998 Aug 27.
18. Creutzfeldt-Jakob disease: decision-making in times of uncertainty. Conference sponsored by Laboratory Centre for Disease Control, Health Canada, in collaboration with McGill Centre for Medicine, Ethics and Law; 1996 June 5-6; Toronto.
19. Conference on CJD: recall, withdrawal, notification and recipient notification. Conference sponsored by Laboratory Centre for Disease Control, Health Canada; 1998 June 1-2; Ottawa.
20. Freedman J. Withdrawals in Canada — What actually happens in a Canadian hospital transfusion medicine department when a notice is received? [lecture]. Conference on CJD: recall, withdrawal, notification and recipient notification. Conference sponsored by Laboratory Centre for Disease Control, Health Canada; 1998 June 1-2; Ottawa.
21. Trevor-Deutsch B. How does a large corporation deal with this question? Bayer's Scientific and Ethical Advisory Committee [lecture]. Conference on CJD: recall, withdrawal, notification and recipient notification. Conference sponsored by Laboratory Centre for Disease Control, Health Canada; 1998 June 1-2; Ottawa.
22. AuBuchon JP, Birkmeyer JD, Busch MP. Safety of the blood supply in the United States: opportunities and controversies. *Ann Intern Med* 1997;127:904-9.

**Reprint requests to:** Dr. Bryce Larke, 8249 – 114 St. NW, Edmonton AB T6G 2R8; fax 403 439-2683; [larkeb@health.gov.ab.ca](mailto:larkeb@health.gov.ab.ca)

**T**he CMA has designed training courses to develop the skills physicians need to access clinical, research and educational information from the Internet.

*INTERNET Level 1: An Introduction for Physicians* is a hands-on course that covers the basics of connecting to the Internet and email discussion groups, and discusses medical resources and the quality of information on the World Wide Web. This course is approved for MOCOMP and MAINPRO-M1 credits.

*OSLER Level 1: Introduction and Intermediate Searching* focuses on searching the databases available through OSLER (OVID Search: Link to Electronic Resources), a service provided free to CMA members. These include MEDLINE, AIDSLINE, CANCERLIT and HealthSTAR. Participants will learn how to find answers to clinical and research questions and how to incorporate literature searches into daily practice. This course is approved for MOCOMP credits and is being assessed for MAINPRO-M1 credits.

## Doctors on the 'Net

### ► *INTERNET Level 1: An Introduction for Physicians*

Ottawa sessions (English): Oct. 7 (afternoon)  
Oct. 20 (morning)  
Oct. 22 (afternoon)  
Ottawa session (French): October (TBA)

### ► *OSLER Level 1: Introduction and Intermediate Searching*

Ottawa sessions (English): Oct. 7 (morning)  
Oct. 20 (afternoon)  
Oct. 22 (morning)

#### **For information or to register:**

CMA Meetings and Travel  
tel 800 663-7336 or 613 731-8610 x 2383  
fax 613 731-8047; [martic@cma.ca](mailto:martic@cma.ca)

#### **For other inquiries or course details:**

Jessie McGowan, Librarian  
CMA Information Services  
tel 800 663-7336 or 613 731-8610 x 2142  
fax 613 731-2076; [mcgowj@cma.ca](mailto:mcgowj@cma.ca)

► **Registration is limited**